REMARKS/ARGUMENTS

Applicants acknowledge receipt of the Office Action dated June 14, 2007. Claims 1-10, 23, and 27-28 are pending in the application. Claims 1, 4-5, 7-9, and 23 have been amended.

In the Office Action, the Examiner rejects claims 1-8, 23, 27 and 28 under 35 U.S.C. §103(a) as being unpatentable over Unger *et al.*, U.S. Patent No. 6,123,923 ("*Unger*") in view of Stahl *et al.*, U.S. Patent No. 5,470,843 ("*Stahl*") or in view of Yan *et al.*, U.S. Patent No. 5,830,539 ("*Yan*"). Applicants believe all pending claims are allowable over the art of record and respectfully request reconsideration and allowance of all claims.

I. Claims 1-8, 23, and 27-28 are patentable over *Unger* in view of *Stahl.*

The Examiner has rejected claims 1-8, 23, and 27-28 under 35 U.S.C. § 103(a) as being unpatentable over *Unger* in view of *Stahl.* Applicants traverse. In order to establish a *prima facie* case of obviousness, the Examiner must meet the following three elements: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings; 2) there must be a reasonable expectation of success; and 3) the prior art reference(s) must teach or suggest all the claim limitations. *MPEP* § 2143 (2005) (citing *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991)). If just one of these elements is not met, the Examiner has failed to establish a case of obviousness. Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness in rejecting claims 1-8, 23, and 27-28.

Claim 1 is an independent claim from which claims 2-10 and 27 depend. Claim 23 is an independent claim from which claim 28 depends. Amended independent claims 1 and 23 recite the limitations, "at least one targeting agent coupled to a fullerene molecule", "at least one linking molecule," "*at least two* antibiotic molecules coupled to the fullerene molecule" and "wherein at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single linking molecule.*" Support for the limitation, "at least two antibiotic molecules coupled to the fullerene molecule" may be found in Figure 2D and original claim 4 of the specification as filed which recited the limitation, "wherein the fullerene-antibiotic conjugate includes at least two antibiotic molecules per C_{60} center." Support for the limitations, "at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single*

linking molecule" may be found, for example, in Figure 2D of the specification as filed which clearly shows two antibiotic molecules coupled to a fullerene molecule via a single linking group, and paragraph [0015], in which it is recited, "forming a malonate or other linking molecule with protected ends, attaching the linking molecule to the fullerene, removing the protective groups from the end(s) of the linking molecule, and affixing the desired bioactive agent to the end(s) of the linking molecule." This paragraph makes clear that at least two bioactive agent molecules may be coupled to the fullerene via a single linking molecule.

Claims 1 and 23 have also been amended to recite targeting agents comprising "at least one selected from the group consisting of bone-targeting moieties, bacteria-targeting moieties, sporulating microbe-targeting moieties, antigen binding sites, and combinations thereof." Support for this limitation may be found, for example, in paragraphs [0033] "a bone-targeted antibiotic", [0042] "bacteria targeting moiety", [0035] "a moiety comprising an antigen binding site, and [0039] "targeting agents for use against sporulating microbes."

Neither *Unger* nor *Stahl* disclose or suggest *at least one targeting agent* and *at least two* antibiotic molecules coupled to the fullerene molecule, nor "wherein at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single linking molecule."*

In particular, section 4 of the Office Action states that "*Unger et al*...discloses a vesicle composition comprising a stabilizing material, a photoactive agent, bioactive agents and/or targeting ligands and their use for therapeutic applications." In this section, the Examiner further states that, "the photoactive agent, fullerene, may be bound to targeting ligands/agents, such as antibodies." The Examiner notes that, "*Unger* does not explicitly disclose binding of the antibiotic to the photoactive agent."

Unger mentions fullerene as a photoactive agent which may be conjugated to an antibody (claim 14 *Unger*). As the Examiner points out however, *Unger* never teaches or suggests coupling a fullerene molecule to an antibiotic molecule. The Examiner cites *Stahl* to make up for the lack of this teaching by *Unger,* but does not cite *Stahl* for teaching the missing limitations: *at least one targeting agent* and *at least two* antibiotic molecules coupled to the fullerene molecule, and "wherein at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single linking molecule."*

The Examiner states in section 5 on page 3 of the Office Action that *Stahl* discloses "the polymer/fullerene may also be directly coupled to a drug moiety, such as antibiotics, erythromycins, etc." As further discussed hereinbelow, Applicants do not agree that *Stahl* teaches a fullerene directly coupled to a drug moiety.

For example, *Stahl* states in the section specifically labeled "Hydrophilic Polymers," column 6 lines 51-57, that "the polymer portion of the compounds of this invention are comprised of at least two identical or different monomer units which are linked together in a linear or branched fashion,....or *in the form of* a ball (e.g., fullerenes)." *Stahl* further states that the *polymer* should be *hydrophilic*. Fullerenes are known to be significantly *hydrophobic*. One of skill in the art, knowing that fullerenes are notably hydrophobic, would not find that *Stahl* teaches a single carbon fullerene molecule, but rather teaches a fullerene-shaped hydrophilic polymer. Moreover, one of skill in the art would not consider a single carbon fullerene molecule a polymer.

Stahl does mention fullerenes as hydrophobic potentiators. However, the potentiator of *Stahl* is linked to a hydrophilic polymer which is linked via a spacer to a carbohydrate portion. Stahl does not teach or suggest that the potentiator, itself is what couples a drug or antibiotic to the hydrophilic polymer. Thus, Applicants submit that *Stahl* does not disclose, as the Examiner suggests, "polymer/fullerene may also be directly coupled to a drug moiety, such as antibiotics, erythromycins, etc." It is clear that *Stahl* is directed only to attaching drugs to functional groups of the hydrophilic polymer portion of the inventive hydrophilic polymer-spacer-carbohydrate molecule. Furthermore, not only does *Stahl* not disclose a fullerene coupled to *an* antibiotic, but *Stahl* clearly does not disclose "*at least two antibiotic molecules* coupled to a fullerene molecule *by a single linking molecule*."

Without conceding the properness of so doing, combining *Unger* and *Stahl* would, as pointed out above, not produce the invention as claimed in amended independent claims 1 and 23. As neither *Unger* nor *Stahl* discloses coupling antibiotic molecules to a fullerene molecule, and furthermore do not disclose *coupling at least two antibiotic molecules* ***and*** *at least one targeting agent to a fullerene molecule* nor *"at least two of the at least two antibiotic molecules being linked to the fullerene* ***via a single linking molecule***," a *prima facie* case of obviousness is lacking. Assuming for the sake of argument that the combination of *Unger* and *Stahl* is proper

(and without conceding such), such a combination does not teach or suggest each and every element of the instant claims 1 and 23, and thus does not make obvious the invention as claimed in the instant amended claims 1 and 23.

Furthermore, contrary to MPEP § 2143, one or ordinary skill in the art would not be motivated to combine *Unger* and *Stahl*. Specifically, MPEP § 2143.01 states that:

> *If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In re Gordon, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).*

As mentioned hereinabove, *Stahl* states, in the abstract and claim 1, for example, that the polymer of his invention must be hydrophilic, in order to produce "carbohydrate-containing polymers which can have an HLB* from about 10 to about 20." The HLB* (lines 20-22 of column 6 of *Stahl*) defines the ratio of the hydrophilic and hydrophobic portions of a molecule using a scale from 1 to 20, with 1 being the most hydrophobic and 20 the most hydrophilic. One of skill in the art, knowing that fullerene is notably hydrophobic, would not be motivated to utilize fullerene as the 'hydrophilic polymer' portion of *Stahl's* carbohydrate-containing polymer. In fact, modifying *Stahl* to use fullerene as the polymer portion of the carbohydrate-containing polymer would render *Stahl* unsatisfactory for its intended purpose, i.e. producing "carbohydrate-containing polymers which can have an HLB* from about 10 to about 20." In addition, *Stahl* acknowledges the hydrophobicity of fullerene when *Stahl* states, "*hydrophobic* substituents are molecules which have a *hydrophobic surface* and which carry reactive functional units, such as, for example, alcohols .... and the *fullerenes*." Thus, according to MPEP 2143.01, there is no suggestion or motivation to modify *Stahl* to use a carbon fullerene molecule as the polymer portion.

Applicants also assert there would be no motivation to modify *Unger* with *Stahl*. *Unger* is directed to encapsulating photoactive agents with stabilizing compounds. The stabilizing compounds may be modified with antibiotics. As it is the Examiner's contention that *Unger* discloses fullerenes as photoactive agents, there would be no reason to modify the photoactive agent with antibiotics as the photoactive agent serves only to act as a contrast agent for imaging

purposes. Accordingly, in view of such teachings, one of ordinary skill in the art would not be motivated to modify *Unger* with *Stahl*.

Applicants therefore submit that the Examiner has not established a *prima facie* case of obviousness in rejecting claim claims 1 and 23, for at least the reason that the cited references do not teach or suggest all of the elements recited in the rejected claims. In addition, since independent claim 1 is submitted to be allowable, dependent claims 2-10 and 27 must *a fortiori* also be allowable, as they carry with them all the limitations of claim 1. Similarly, since independent claim 23 is submitted to be allowable, dependent claim 28 must *a fortiori* also be allowable for at least the reasons set forth with respect to claim 23, as claim 28 comprises all the limitations of claim 23. Accordingly, Applicants respectfully request that the Examiner withdraw the § 103 rejections of claims 1-10, 23, and 27-28.

II. Claims 1-8, 23, and 27-28 are patentable over *Unger* in view of *Yan*.

The Examiner has further rejected claims 1-8, 23, and 27-28 under 35 U.S.C. § 103(a) as being unpatentable over *Unger* in view of *Yan*.

As mentioned in Section I hereinabove, *Unger* fails to disclose "*at least one targeting agent*" and "*at least two antibiotic molecules*" coupled to the fullerene molecule. Furthermore, *Unger* fails to disclose the limitation, "wherein at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single linking molecule.*"

As pointed out above and by the Examiner in section 4 on page 3 of the Office Action, *Unger* does not disclose binding of an antibiotic to the photoactive agent. *Yan* is cited to make up for this lack of teaching by *Unger*, but is not cited by the Examiner for teaching or suggesting the following limitations of claims 1 and 23, which are also not disclosed by *Unger*: "*at least one targeting agent*" and "*at least two antibiotic molecules coupled to the fullerene molecule;*" and "wherein at least two of the at least two antibiotic molecules are coupled to the fullerene molecule *via a single linking molecule*."

The Examiner states in section 6 on page 4 of the Office Action that, "*Yan et al.* discloses the method for coating or functionalizing a substrate, such as a fullerene with a first layer comprising a molecular tether covalently bonded to the surface and a second layer comprising antibiotics bonded to the first layer." The Examiner continues, by stating that, "the fullerene may be further functionalized with targeting ligands, such as antigens, etc."

Yan, column 6 lines 35-40, discloses a method for coating a workpiece via "applying a reagent comprising molecules each having a nitrenogenic group and *a* functional group to a workpiece. The workpiece is then exposed to a reaction energy source so as to convert the nitrenogenic groups to nitrenes which undergo addition and/or insertion reactions with chemical moieties on the workpiece, thereby attaching the reagent to the workpiece. *A* biomaterial is then coupled to *the* functional group." In column 6 lines 29-32, *Yan* states that, the workpieces may be "devices made from polymeric materials, such as.....and C_{60}." In claims 4 and 12, *Yan* states that "*a* nucleophile" may be coupled to the substrate and in claims 5 and 13, *Yan* states that "*the* nucleophile" may be an antibody.

The "*workpiece*" of *Yan* is ***not*** "a *fullerene molecule*." Instead, *Yan* is directed to coating substrates such as portions of medical devices with a functionalized coating. *Yan*'s primary purpose is functionalizing large surfaces of a workpiece for the attachment of bioactive molecules. Nowhere does *Yan* contemplate or suggest coating an individual fullerene molecule. Nor does *Yan* teach or suggest how such a process could be accomplished. *Yan* never discloses, as in the instant claims 1 and 23, coupling *at least two* antibiotic molecules ***and*** *at least one* targeting agent *to* ***a*** *fullerene molecule*. Furthermore, *Yan* never discloses, as in the instant claims 1 and 23, "*at least two* of the at least two antibiotic molecules *being linked to the fullerene via a single linking molecule*."

Yan, therefore, fails to make up for the lack of teaching by *Unger*. Because *Unger* and *Yan* fail to disclose each and every element of the instant independent claims 1 and 23, the combination of *Unger* and *Stahl* fails to make obvious the claims. As such, it is respectfully requested that the 35 U.S.C. §103(a) rejections to claims 1 and 23 be removed, and claims 1 and 23, as well as claims 2-10 and 27, and 28, respectively depending therefrom, be removed and the claims allowed.

III. Other Amendments

Claim 4 has been amended to recite, "the fullerene-antibiotic conjugate according to claim 2 wherein the conjugate comprises from two to eight linking molecules, wherein at least one linking molecule couples at least two antibiotic molecules to the fullerene molecule." Support for this amendment may be found in paragraph [0047] of the specification as filed which recites, "up to 8 malonate groups can be placed on C_{60}."

Amended claim 5 recites, "The fullerene-antibiotic conjugate according to claim 2 wherein the conjugate includes at least three antibiotic molecules per C_{60} center, at least two of the at least three antibiotic molecules coupled to the fullerene molecule via a single linking molecule. Support for this amendment to claim 5 may be found in originally filed claim 5 which recited, "the fullerene-antibiotic conjugate ... wherein the conjugate includes at least three antibiotic molecules per C_{60} center" and paragraph [0049], in which it is stated, "in some instances, the attachment of multiple antibiotics is preferred. For example, conjugates containing less than three vancomycin per C_{60} may have low solubility in water."

Claim 8 has been amended to recite the limitation, "wherein the at least one targeting agent is selected from the group consisting of targeting agents comprising at least one antigen bonding site selected from the group consisting of targeting agents derived from antibodies against anthrax and antibodies against anthrax spores." Support for this amendment may be found in paragraph [0039], which recites, "exemplary targeting agents include, but are not limited to, those derived from antibodies against anthrax or other bacteria, antibodies against the spores of anthrax or other bacteria."

Amended claim 9 recites, "the conjugate according to claim 1, wherein the at least one targeting agent comprises a bone-targeting moiety." Support for this amendment is found, for example, in paragraph [0042] of the specification as filed, which recites, "the targeting agent may be a bone targeting moiety."

Claim 7 has been amended to recite, "the conjugate according to claim 9, wherein the at least one targeting agent comprises diphosphonate." Support for this amendment is found in paragraph [0033] of the specification as filed, which states, "a bone-targeted antibiotic might also be prepared using a similar reaction scheme, by condensing vancomycin or other suitable antibiotic with an aminodiphosphonate derivative, such as 3-amino propylene-diphosphonic acid."

IV. Conclusion

Applicants respectfully request reconsideration, allowance of the claims, as amended, and a timely Notice of Allowance be issued in this case. If the Examiner feels that a telephone conference would expedite the resolution of this case, the Examiner is respectfully requested to contact the undersigned.

In the course of the foregoing discussions, Applicants may have at times referred to claim limitations in shorthand fashion, or may have focused on a particular claim element. This discussion should not be interpreted to mean that the other limitations can be ignored or dismissed. The claims must be viewed as a whole, and each limitation of the claims must be considered when determining the patentability of the claims. Moreover, it should be understood that there may be other distinctions between the claims and the prior art that have yet to be raised, but which may be raised in the future.

If any fees are inadvertently omitted or if any additional fees are required or have been overpaid, please appropriately charge or credit those fees to Conley Rose, P.C. Deposit Account Number 03-2769.

Respectfully submitted,

Date: September 28, 2007

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